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Review Article

The effect of intravitreal injection on macular thickness on visual acuity and status of intra ocular pressure with diabetic macular edema

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ABSTRACT

Aim: Intravitreal ranibizumab injection very common in treatment of diabetic macular edema also helpful in decreasing the changes caused due to Diabetic Macular Edema, associated with different types of diabetes and works well in overall improvement of visual outcomes. To assess changes in macular thickness using OCT MACULA and intraocular pressure using a noncontact tonometer (NCT) before and after intravitreal ranibizumab injection in diabetic macular edema patients.

Materials and Methods: This was observational study done on 60 patients. The assessment of macular thickness changes done with the help of optical coherence tomography (OCT) and intraocular pressure monitored with non-contact tonometer (NCT) whereas visual acuity assessment was recorded with Snellen's chart. Intravitreal injection of 1.25 mg of Ranibizumab was injected 3.5 mm from the limbus under topical anaesthetic drops. Post injection follow up was scheduled on 1st post procedure day and after one month. Post procedure Optical coherence tomography (OCT) was performed in all patients 1 week before and 1 month after 1st injection

Result: Out of a total of 60 eyes, 38 patients had poor control of diabetes, whereas in 22 (64%) patients' diabetes was under control with treatment. IOP recorded had a mean value of 17mmHg in 95% of cases and 5% had gone to higher side 30mmHg to 45mmHg. The mean Central Macular Thickness pre intravitreal Ranibizumab injection thickness was 385.40 ± 42.25 μ m. After giving injection, on the final visit after 1 month, the mean thickness had gradually decreased by 324.22 ± 33.55 μ m. 53 patients out of 60 (88%) had Insulin Dependent Diabetic Mellitus whereas 7 cases (12%) had Non-Insulin Dependent Diabetic Mellitus

Conclusion: Ranibizumab intravitreal injection is effective in cases of DME. This is also effective to improve visual outcome. NPDR was most commonly found in Insulin Dependent Diabetic Mellitus and in cases of Proliferative diabetic Retinopathy -Non-Insulin Dependent Diabetic Mellitus was more commonly observed. Central macular thickness after 1 month of injection was reduced in 57 cases 95% whereas the visual acuity improvement also seen in these patients and increased. In 57 / 60 cases (95%) visual acuity was improved, In 2/60 (3.34%) visual acuity remained as it is and in 1/60 (1.66%) case it was decreased. In 95% of cases the IOP maintained under normal limits. In 5% cases it had gone to the higher side.

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1. Introduction

Diabetic macular edema (DME) is one of the most common causes of visual impairment in diabetic patients with diabetic retinopathy. Risk factors for DME include chronic

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diabetes, high systolic blood pressure, and high HbA1C. The ocular component connected to DME is the severity of diabetic retinopathy. As the severity rises, so does the prevalence of DME. The prevalence of DME in persons with diabetic retinopathy varies from 2.7% to 11% depending on the type and duration of diabetes. The macular thickness increases in DME is a result of an increase in extracellular fluid produced by hyperpermeable retinal capillaries. Additionally, persistent hyperglycaemia results in leukocyte stasis, elevated VEGF levels in the retina, increased venous dilation, decreased oxygen tension in the inner retina, dysregulated growth factor levels, and elevated serum exudation from the retinal vasculature into the extracellular space. Diabetic retinopathy is mostly brought on by uncontrolled diabetes mellitus, but it can also be brought on by poor blood flow, retinal disease, and inflammations.¹ Detection and control the methods for detecting DME include stereoscopic slit lamp examination, SD OCT, fundus imaging, and fluorescein angiography. The first step in the diagnosis of DME is a slit-lamp examination of the posterior pole, which determines the presence and location of macular thickness, exudates and cystoid abnormalities. For evaluating and grading diabetic retinopathy, the Early Treatment Diabetic Retinopathy Study (ETDRS) classification system, which employs a classified way of documenting the disease severity and clinical data on each visit, is helpful.² The increased prominence of qualitative and quantitative assessments of structural changes in the macula made available by OCT has been beneficial for DME diagnosis, therapy, and follow-up. According to, OCT results are quite accurate at detecting any increase in macular thickness over the prior measurement, beyond OCT measurement variability, and tracking real change. Diagnostic, localization, and management tools for DME now include fundus photography and angiography. When fluorescence or indocyanine green dye is intravenously injected for fundus angiography, it is a useful tool for detecting changes in the intravascular and extravascular compartments of the retina and choroid.³ The FDA has approved the use of ranibizumab intravitreal injection as a safe and effective treatment for DME. It binds to the VEGF A receptor binding site and prevents all VEGF molecules from attaching to their receptors on the surface of endothelial cells.⁴ Giving the patient steroids, such as fluocinolone acetonide, dexamethasone, or triamcinolone, which can be administered intravitreally without the need of preservatives, is another way to treat DME. Cataracts, increase in intraocular pressure, and possibly implant migration are complications that can arise from implants.⁵ Poor visual outcomes are also caused by signs and symptoms of DME, such as blurry vision in the affected eye, wavy vision, mismatched image formation, dull or dusky vision, dark lines or patches in the field of vision, and scotomas.⁶ Diagnosis Investigative techniques: Slit lamp

Observation using a 90 D/78D lens in dilated patients, DME can be identified and macular thickness is readily seen. For the assessment of the retina's central region, 78D is helpful. In contrast, the 90D's lens magnifies by 0.76x and provides a reduced view of the retina.⁷ IDO test for indirect ophthalmoscopy. When compared to a slit lamp fundus examination, this test is more thorough. This is carried out binocularly while the patient is supine. It provides an enlarged, expansive picture of the fundus.⁸ Laser Coherence Tomography it is a diagnostic procedure to check the health and state of the retinal layers. This test is helpful in DME situations to assess the measurements of retinal thickness caused by edema. The mitigation of DME necessitates stringent blood pressure and blood sugar control. Although an individual also needs to change their diet and monitor their weight, anti-VEGF agents including ranibizumab, bevacizumab, aflibercept, brolucizumab, and faricimab were developed years ago and are the first line of treatment. Ranibizumab and aflibercept were approved by the FDA in 2005. Brolucizumab and faricimab were also approved, and bevacizumab has been used off-label for several ocular disorders. Not all treatments are totally effective at managing DME resolution. The body may react differently to different treatments. Switching to another anti-VEGF medication is a possibility when the eyes do not respond.⁹

2. Materials and Methods

Patients with DME who presented to the ophthalmology outpatient department at Sangam Netralaya, Mohali were enrolled in this observational study after taking written informed consent. The Eye Hospital's outpatient department examined the sixty eyes of the sixty patients who made up the sample size.

Under topical anaesthetic drops, 1.25 mg of ranibizumab was injected intravitreally through the pars plana. On the first post-procedure day and one month post-injection follow-up appointments were planned. OCT was taken one week prior to the initial injection and one month after. Complications in DME causes a progressive and permanent loss of vision. Endophthalmitis is one of the complications after intravitreal injection. Vitreous hemorrhage, cataracts, and improper injection technique cause an unchecked rise in intraocular pressure, which causes retinal tears and central retinal vein blockage.⁹

3. Results

Sixty eyes from sixty individuals were studied over a six-month period, 32 of the patients were men (54%) and 28 were women (46%). Participants in this study had been given a DME diagnosis. ranging from 45 to 93 years old. While 53 people had diabetes and were taking insulin (IDDM) rest 7 had non-insulin dependent diabetic mellitus

(NIDDM). The 24 cases had NPDR in 34 eyes and PDR in the remaining 26. Out of 60 eyes, 38 had poorly controlled diabetes, whereas 22 patients' diabetes was under control as they were regular to their medication (36%) IOP variations typically have a mean value of 17 and only 5% of the time do they show fluctuations to the higher side. The average thickness before intravitreal Ranibizumab injection was $385.40 \pm 42.25 \mu\text{m}$. Following injection on the last visit, the mean thickness was gradually shown to decrease by $324.22 \pm 33.55 \mu\text{m}$ (CMT). After one month of injections, the central macular thickness was reduced in 57 cases by 95%, but these patients also observed an enhancement in their visual acuity. That was 3.34% in 2 instances. These 3.34% of patients had no change in their visual acuity, and only one had a decline (1.66%).

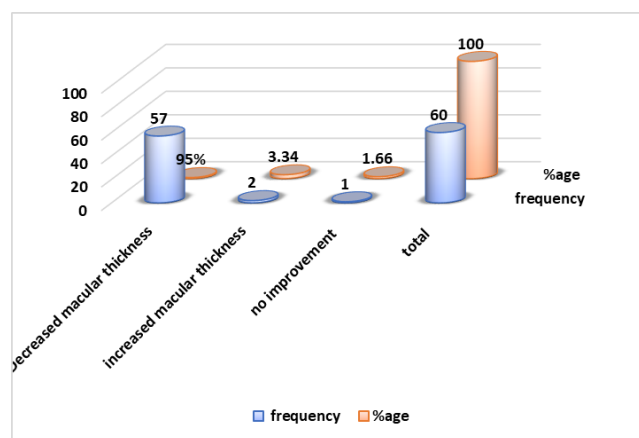


Figure 2: Mean pre intravitreal Ranibizumab injection thickness was $385.40 \pm 42.25 \mu\text{m}$. After giving injection on the final visit after 1 month showed mean thickness were seen gradually decreased by $324.22 \pm 33.55 \mu\text{m}$

4. Discussion

In previously published studies the examination of visual outcome, central macular thickness, fundus patterns were observed as mentioned below. VEGF orchestrates the breakdown of the blood-retinal barrier, leading to increased vascular permeability. As a consequence, retinal edema ensues, compromising visual function. In the case of DME, VEGF runs rampant, exacerbating fluid accumulation within the macula.¹⁰ The unconventional path leads us to intravitreal ranibizumab. Not all treatments are totally effective at managing DME resolution. The body may react differently to different treatments. Switching to another anti-VEGF medication is a possibility when the eyes do not respond to the prior one. This article gave more clarity on intra ocular pressure visual acuity and most importantly the presence of type of diabetic retinopathy with respect to insulin and non-insulin dependent diabetic mellitus. In a study by Amitha et al., the goal was to examine the visual

outcomes in Diabetic Macular Edema patients.¹¹ They enrolled seven fifty-nine patients with Diabetic Macular Edema who had Central Macular Thickness $> 275 \mu\text{m}$ and were given monthly intravitreal ranibizumab injections of 0.3 or 0.5 mg. They were examining changes in hard exudates and visual acuity, but the results showed that there was no correlation between hard exudates and visual acuity.¹² They came to the conclusion that there was no connection between Visual Acuity and hard exudates. Twenty three out of Thirty-three individuals in the study by Arevalo et al. had Insulin Dependent Diabetic Mellitus, while the other ten had Non-Insulin Dependent Diabetic Mellitus.¹³ Sixty patients, sixty eyes ranging from forty-five to ninety-three years old while thirty-eight people had diabetes and were taking insulin (Insulin Dependent Diabetic Mellitus), the remaining twenty four people had Non Proliferative Diabetic Retinopathy in thirty four eyes and Proliferative Diabetic Retinopathy in the remaining twenty-six eyes. A disorder known as diabetic macular edema causes the macula's thickness to increase, which disrupts Visual Acuity variations in intraocular pressure and causes issues with vision. This is a result of the diabetes's poor control and protracted history. This study demonstrates that visual acuity increases as thickness decreases, with Intra Ocular Pressure variations having a mean value of 17 in 95% of cases and larger fluctuations in 5% of patients that were treated with Mannitol Intra Venous after injection. Ranibizumab injection lowers edema and has positive effects on the appearance¹⁴ whereas after giving Mannitol Intra venous the intra ocular pressure in five cases it increased by 30mmHg- 40mmHg. This sudden rise in IOP warrants attention and further investigation While ranibizumab effectively reduces macular edema, the interplay between treatment and IOP dynamics requires careful monitoring. Mannitol, a hyperosmotic agent, may play a role in these fluctuations, but its precise mechanism remains an area of interest. Mitigation of Intra Ocular Pressure patterns were observed in this research as not been discussed in previously published papers.¹⁵ Many articles were previously published showed improvement in central macular thickness, decrease in macular edema and improvement in visual functioning after reduction. Our study was aimed to focus on different parameters ocular parameters in one article which included visual outcome, patterns of intra ocular pressure, presence of Proliferative and non-proliferative diabetic retinopathy commonly found in different types of Diabetic mellitus which were Insulin dependent and non-insulin dependent diabetic mellitus.¹⁶ Twenty eyes with DDME that had not reacted to prior photocoagulation were treated with IVB at a dose of 1.25 mg, according to data reported by Kumar and Sinah¹⁹. They came to the conclusion that, after three months, IVB significantly reduced macular thickness and improved BCVA. Out of 30 eyes, Ozkiris A20's results showed that

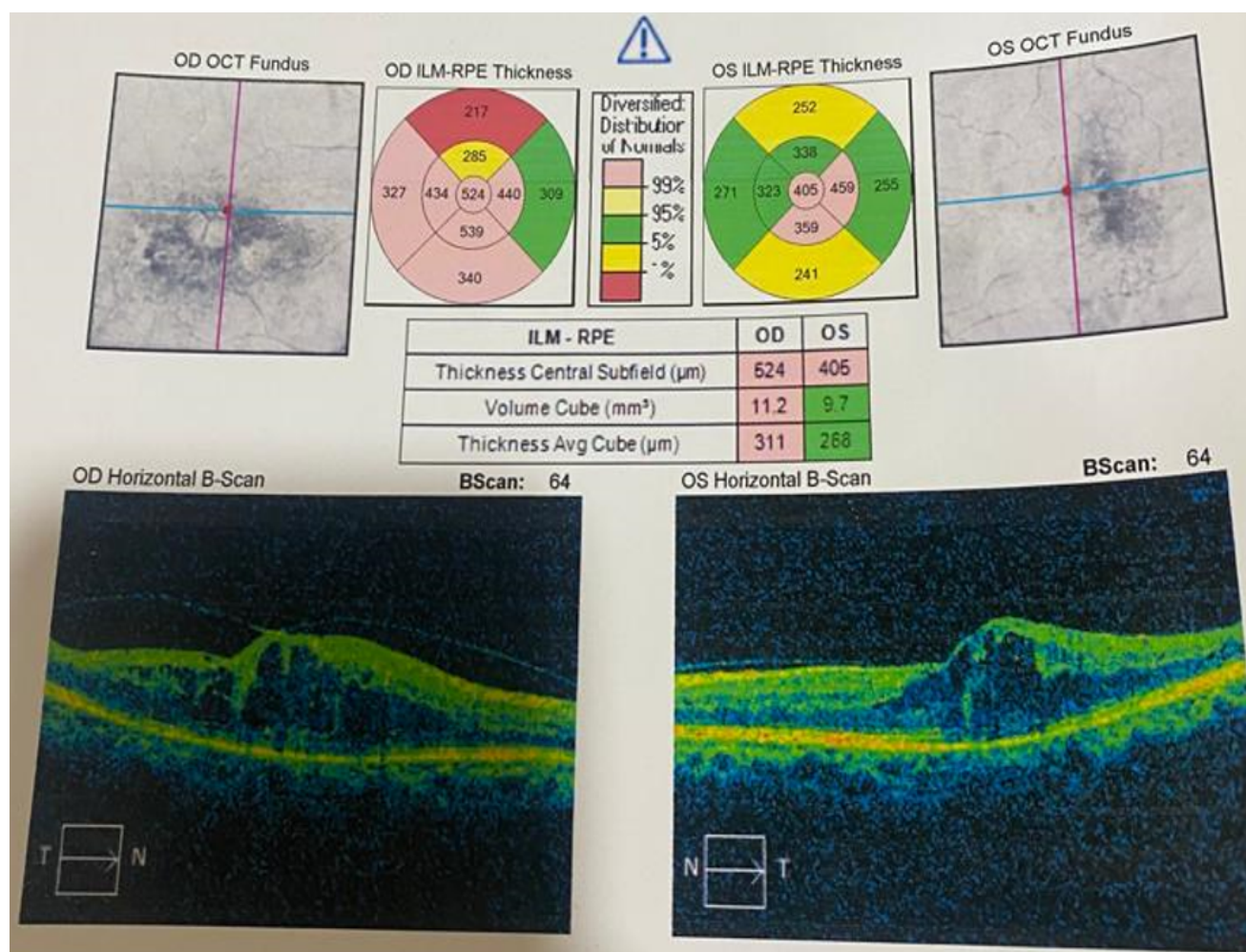


Figure 1: Optical coherence tomography and macular edema

24 (80%) of the eyes had improved visual acuity following an average follow-up period of 5.6 months following IVB injection. Whereas in our research Central macular thickness after 1 month of injection was reduced in 57 cases 95% whereas the visual acuity improvement also seen in these patients and increased. In 57 / 60 cases (95%) visual acuity was improved, in 2/60 (3.34%) visual acuity remained as it is and in 1/60 (1.66%). case it was decreased.¹⁷

It was observed in our research that it is most usual to find NPDR in cases of Insulin Dependent Diabetic Mellitus and Non-Insulin Dependent Diabetic Mellitus in cases of Proliferative Diabetic Retinopathy. After receiving an injection, the central macular thickness decreased in 57 cases, or 95% of the cases, while the patients' visual acuity also improved and rose got better.

5. Future Prospective

Further research is needed to explore the interplay between IOP, Patterns with respect to the type of intravitreal injection in different type of DM along with macular thickness, and visual outcomes.

To better assess a certain age group's effectiveness throughout the early phases of DME. Injections of ranibizumab into the eye are successful in treating DME. This works well to enhance the visual result. The most frequent occurrence of NPDR is in cases with IDDM, while NIDDM is more frequently seen in PDR cases. After one month of injections, the central macular thickness was reduced in 57 cases by 95%, but these patients also observed with enhancement in their visual acuity. The visual acuity of these 3.34% patients in 2 cases remained the same and in 1 case it deteriorated (1.66%).

6. Source of Funding

None.

7. Conflict of Interest

None.

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